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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/659,599	09/11/2000	Glenn H. McGall	2719.2001-000	4766

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EXAMINER	
EPPS, JANET L	
ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/659,599	MCGALL, GLENN H.	
	Examiner	Art Unit	
	Janet Epps	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 30-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 30-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 September 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Arguments

1. Applicant's arguments with respect to claims 1-23 have been considered but are moot in view of the new ground(s) of rejection.

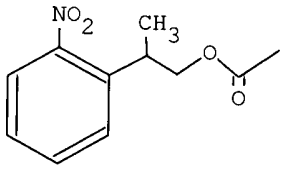
Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Pfleiderer et al. (WO: 96/18637 A2 or US: 5763599).

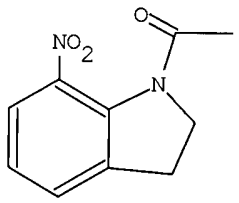
Pfleiderer et al. dislose methods for the preparation of nucleoside derivatives with photolabile protecting groups. In one particular embodiment, Pfleiderer et al. discloses the compound Thymidine, 5'-[2-(2-nitrophenyl) propyl carbonate] (see Example 10). This compound corresponds to M-Y1 as claimed in the present invention wherein M is a nucleoside, and Y1 has the following formula:



Furthermore, in one embodiment of this reference, Pfleiderer et al. teach that the compounds according to the present invention may comprise 3' protected ribofuranosides, wherein said 3' position is protected with known phosphoramidite groups (col. 4, lines 33-40).

Pfleiderer et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

4. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Papageorgiou et al. This reference discloses a glutamate residue modified with a group of the following formula:



The group is modified in the benzyl ring with a substituted alkyl group in the meta position with respect to the nitro group (see page 6503, scheme 1, compound 10).

Papageorgiou et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pfleiderer et al. in view of Fodor et al. or McGall et al. (5,412,087)

The teachings of Pfleiderer et al. set forth above are incorporated here.

In regards to the claimed methods, Pfleiderer et al. teach the use of modified nucleosides in a method adopted by Fodor et al. (1991). Pfleiderer et al. further teach that their disclosed compounds are extremely suitable for the preparation of oligonucleotides by cleaving the protective groups in a light controlled manner, particularly on solid carrier plates (col. 4, lines 61-65). The nucleoside derivatives of Pfleiderer et al. can be deprotected very quickly and extensively using polychromatic light having a wavelength of greater than 289 nm (col. 4, lines 55-60).

However, this reference does not expressly provide wherein the photolabile groups are removed by using wavelengths of greater than 350 or 365 nm, methods of attaching a molecule represented by the formula M_1-Y_1 to a support, or a method of forming, from component molecules represented by formula M_1-Y_1, a plurality of compounds bound to a support. Additionally, Pfleiderer et al. does not teach wherein the solid support comprises regions having an area of between 1 μm^2 and 10,000 μm^2.

Fodor et al. provides a method for light directed synthesis of oligonucleotides (bridging paragraph, pages 771-772, Figure 8.) The method of Fodor et al. comprises attaching a nucleoside monomer covalently linked to a photolabile group to the surface of a glass substrate. The protecting group, in this case 5'-Nitroveratryl, was then removed by illumination, and the substrate (Thymidine) was then treated with a phosphoramidite-activated derivative of deoxycytidine.

McGall et al. provide methods and compositions of matter are provided for immobilizing oligonucleotides and other biological polymers on predefined regions of a surface of a solid support. The methods involve activating regions of a surface by attaching to the surface a thiol

functional group protected with a photochemical protecting group so that the thiol has very low reactivity for other functional groups reactive with thiols. The protected thiol is convertible by irradiation to a fully reactive thiol capable of immobilizing a desired biological polymer such as a nucleic acid, protein, or polysaccharide. Predefined regions of the surface are selectively irradiated to convert the protected thiols in the predefined regions to reactive thiol groups. The desired biological polymers subsequently can be immobilized on the activated regions of the surface. The methods taught by McGall et al. allows for the formation of patterned surfaces having preselected reactivities. For example, by using lithographic techniques known in the semiconductor industry, light can be directed to relatively small and precisely known locations on the surface. Thus, the present invention can be used to activate discrete, predetermined locations on the surface for attachment of biological polymers. The resulting surface will have a variety of uses. For example, in one embodiment, the method involves the light-directed immobilization of oligonucleotides on a glass surface derivatized with a caged thiol reagent. The method can be used to fabricate large arrays of oligonucleotide probes (col. 3, lines 1-45).

The caging groups used in the methods of McGall et al. are preferably photoactivatable. Preferably, the photosensitive cages will be activatable by low energy ultraviolet or visible light. Many, although not all, of the photosensitive protecting groups are aromatic compounds. More preferably, the photosensitive protecting group will be a nitro benzylic compound, such as o-nitrobenzyl or benzylsulfonyl groups. In a preferred embodiment, 6-nitroveratryloxycarbonyl (NVOC); 6-nitropiperonyloxycarbonyl (NPOC); alpha, alpha-dimethyldimethoxybenzyloxy-carbonyl (DDZ), methyl 6-nitroveratryloxycarbonyl (MenVOC), methyl-6-nitropipe

ronyloxycarbonyl (MeNPOC), or 1-pyrenylmethyl is employed. McGall et al. further state that many photosensitive protecting groups are suitable for use in their method.

McGall et al. in regards to regions of the solid support utilized in their disclosed methods, once the surface is covered with a plurality of caged thiol groups, selected regions of the surface may be irradiated to provide free thiols on the surface. In a preferred embodiment, the radiation is UV, near IR, or visible light. The light source may be coherent or noncoherent. In some embodiments, the exposed area is less than about 1 cm^2 or less than about 1 mm^2. In preferred embodiments the irradiated area will be composed of a pattern of smaller, discrete irradiated areas, each of which is less than about 10,000 μm^2or, more preferably, less than about 100 μm^2. Preferably, each individual synthesis site in the pattern is about 50 to 500 μm^2. Spaces between activated regions are not critical and will generally be greater than about 1 μm^2. Exposure of the surface to light will typically be carried out with a suitable mask using photolithographic techniques well known in the semiconductor industry (col. 8, lines 50-65). McGall et al. further teach the use of wavelengths between 280 and 420 nm in their methods (see Table 1, col. 8).

It would have been obvious to one of ordinary skill in the art at the time of filing to modify the teachings of Pfleiderer et al. with the teachings of Fodor et al. since Pfleiderer et al. clearly states that their disclosed nucleoside derivatives are extremely suitable for the preparation of oligonucleotides, particularly in the methods described by Fodor et al. (col. 28, lines 23-33). One of ordinary skill art at the time of filing would have been motivated to combine the compounds of Pfleiderer et al. with method disclosed by Fodor et al. since Pfleiderer et al. teach that by following the methods set forth in Fodor et al. they were able to achieve an uncomplicated synthesis of oligonucleotides with very high yields, with the result that they are

suitable in practice for light-controlled parallel synthesis of oligonucleotides (col. 28, lines 30-33). Additionally, it would have been obvious to one of ordinary skill in the art to modify the teachings Pfleiderer et al. with the teachings of McGall et al. in the design of method for synthesizing oligonucleotides according to the present invention. It would have been obvious since McGall et al. clearly teach that nitro-benzyl photosensitive groups are particularly suitable for use in their disclosed methods, and the photosensitive groups disclosed in Pfleiderer et al. are nitro-benzylic type compounds. One of ordinary skill in the art seeking alternative methods for synthesizing oligonucleotides, would have been motivated to substitute one functionally equivalent photosensitive (or photolabile) group, as disclosed in the prior art as useful for the same purpose, for another equivalent photosensitive group.

Therefore, the invention as a whole would have been *prima facie* obvious over Pfleiderer et al. in view of Fodor et al. or McGall et al.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 7-12, and 30-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites "wherein Y1 and M of the second molecule are selected independent of the first molecule." The metes and bounds of the phrase "selected independent of" as used in this context is vague and indefinite since it is unclear if the Y1 group in the second molecule is to be selected from the "group consisting of" set forth in claim 5, or if other Y1 groups independent

from this group are encompassed in this definition of Y1. Additionally, claim 8 recites "molecules represented by the formula M-Y1, wherein Y and M for each occurrence are selected independently." This phrase is also vague and indefinite since is unclear what the phrase "selected independently" is intended to encompass since the definitions of M and Y1 are obviously independent of each other, and further it is unclear if groups other than those defined in claim 5 are encompassed in the definitions of both M and Y1.

Claim 30 recites the formula M-Y_1, however this claim only provides a definition for the term Y_1. There is no definition for the M term in this formula, therefore the metes and bounds of the structure of the formula of the compounds recited in this claim are vague and indefinite. Additionally, one of the compounds recited in claims 30-31 that correspond to Y1 comprise the term "R", however there is no definition provided for this term.

Claims 32-33 recite various compounds which correspond to Y_1, however the Y_1 compounds recited in claims 32-33 lack antecedent basis since the Y_1 compounds defined in claims 5 and 8 do not correspond to those set forth in the instant claims.

Claims 34-35 recites various compounds that correspond to Y_1, however the Y_1 compounds recited in the instant claims lack antecedent basis in claim 14 since the Y_1 compounds defined in claim 14 do not correspond to those set forth in the instant claims.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 8:30AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps
Examiner
Art Unit 1635

JLE
March 11, 2002

SEAN McGARRY
PRIMARY EXAMINER